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(FILE 'HOME' ENTERED AT 13:22:22 ON 08 AUG 2003)

FILE 'CAPLUS' ENTERED AT 13:22:31 ON 08 AUG 2003

L1 3 S CANCER AND P53 WILD TYPE PROTEIN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIODBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 13:24:44 ON 08 AUG 2003

L2 39 S CANCER AND P53 WILD TYPE PROTEIN

L3 17 DUP REM L2 (22 DUPLICATES REMOVED)

L4 3 S L3 AND ANTICANCER AGENT

L5 2 S CANCER WITH P53 PROTEIN AND ANTICANCER DRUG

L6 140522 S CANCER (P) P53

L7 33004 S L6 AND (ANTICANCER OR CHEMOTHERAPY OR CHEMOTHERAPEUTIC OR N

L8 10192 S L7 AND (P53 (P) INCREAS?)

L9 6529 S L8 AND (AGENT OR DRUG OR COMPOUND)

L10 406 S L9 AND PD<1997

L11 206 DUP REM L10 (200 DUPLICATES REMOVED)

=>

AN 2000:383903 CAPLUS
 DN 133:26844
 TI Methods and compositions using hydrophobic group- and cationic
 group-containing compounds for restoring conformational stability of a
 protein of the p53 family
 IN Coffey, Heather Anne; Connell, Richard Damian; Foster, Barbara Ann;
 Rastinejad, Farzan
 PA Pfizer Products Inc., USA
 SO PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 1-6 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032175	A2	20000608	WO 1999-IB1916	19991201
	WO 2000032175	A3	20000803		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1998-110542	P	19981202		
OS	MARPAT 133:26844				
AB	The invention provides pharmaceutical compds. capable of interacting with mutant and nonmutant forms of cancer-related regulatory proteins such that the mutant protein regains the capacity to properly interact with other macromols., thereby restoring or stabilizing all or a portion of its wild type activity. Regulatory proteins include members of the p53 protein family, e.g. p53, p63 and p73. The compds. of the invention are useful for cancer treatment. Methods for screening for such pharmacol. compds. are also provided. Compds. of the invention contain a hydrophobic group (e.g. a planar polycyclic group) and a cationic group (preferably an amine) joined by a linker.				
ST	polycyclic amine compd p53 conformation stabilization; cancer treatment p53 conformation stabilizing compd; screening antitumor p53 conformation stabilizing compd				
IT	Protein motifs (DNA-binding domain; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)				
IT	DNA RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (DNA-binding domain; hydrophobic group- and cationic group-contg.)				

comps. for restoring p53-family protein conformational stability)

IT Animal cell line
(H1299; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Animal cell line
(SaOS-2; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Antitumor agents
(carcinoma, DLD-1 cell; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(damage; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Temperature effects, biological
(heat, p53 DNA-binding domain thermolability; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Alleles
Antitumor agents
Molecular association
Mutation
Stabilizing agents
Structure-activity relationship
(hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT p53 (protein)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Antitumor agents
(melanoma, A375.S2 cell; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Mutation
(missense; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Cyclin dependent kinase inhibitors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p21CIP1/WAF1; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

for

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p63; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p73; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Conformation
(protein; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT 58-40-2 84-96-8 13365-37-2 36945-50-3 74151-33-0 103395-43-3
127136-38-3 259199-65-0 259199-66-1 273921-61-2
273921-62-3 273921-63-4 273921-64-5 273921-65-6 273921-66-7
273921-67-8 273921-68-9 273921-69-0 273921-70-3 273921-71-4
273921-72-5 273921-73-6
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

AN 2000:6873 CAPLUS

DN 132:175329

TI Pharmacological rescue of mutant p53 conformation and function

AU Foster, Barbara A.; Coffey, Heather A.; Morin, Michael J.; Rastinejad, Farzan

CS Department of Genomics, Targets, and Cancer Research, Pfizer Central Research, Groton, CT, 06340, USA

SO Science (Washington, D. C.) (1999), 286(5449), 2507-2510
CODEN: SCIEAS; ISSN: 0036-8075

PB American Association for the Advancement of Science

DT Journal

LA English

CC 1-3 (Pharmacology)

AB Compds. that stabilize the DNA binding domain of p53 in the active conformation were identified. These small synthetic mols. not only promoted the stability of wild-type p53 but also allowed mutant p53 to maintain an active conformation. A prototype compd. caused the accumulation of conformationally active p53 in cells with mutant p53, enabling it to activate transcription and to slow tumor growth in mice. With further work aimed at improving potency, this class of compds. may

be developed into anticancer drugs of broad utility.

ST CP31398 CP257042 p53 gene activation antitumor; conformation DNA binding domain p53 antitumor

IT Conformation
(DNA; pharmacol. rescue of mutant p53 conformation and function)

IT Gene, animal
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(TP53; pharmacol. rescue of mutant p53 conformation and function)

IT Structure-activity relationship
(antitumor; pharmacol. rescue of mutant p53 conformation and function)

IT Antitumor agents
(pharmacol. rescue of mutant p53 conformation and function)

IT 259199-65-0, CP 31398 259199-66-1, CP 257042
RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)
(pharmacol. rescue of mutant p53 conformation and function)

RE.CNT 27

RE

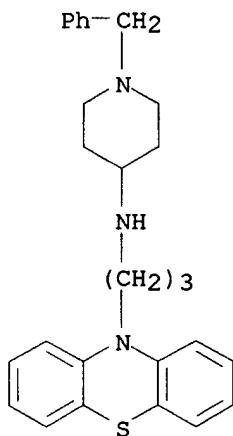
- (1) Bartek, J; Oncogene 1990, V5, P893 CAPLUS
- (2) Bullock, N; Proc Natl Acad Sci USA 1997, V94, P14338
- (3) Chen, J; Oncogene 1993, V8, P2159 CAPLUS
- (4) Cho, Y; Science 1994, V265, P346 CAPLUS
- (5) Daniels, D; J Mol Biol 1994, V243, P639 CAPLUS
- (6) Euhus, D; J Surg Oncol 1986, V31, P229 MEDLINE
- (7) Foster, B; data not shown
- (8) Friedlander, P; J Biol Chem 1996, V271, P25468 CAPLUS
- (9) Gamble, J; Virology 1988, V162, P452 CAPLUS
- (10) Hainaut, P; EMBO J 1992, V11, P3513 CAPLUS
- (11) Halazonetis, T; EMBO J 1993, V12, P1021 CAPLUS
- (12) Hollstein, M; Nucleic Acids Res 1994, V22, P3551 CAPLUS
- (13) Hupp, T; Cell 1995, V83, P237 CAPLUS
- (14) Kern, S; Science 1991, V252, P1708 CAPLUS
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- (16) Milner, J; Oncogene 1990, V5, P1683 CAPLUS
- (17) Miroy, G; Proc Natl Acad Sci USA 1996, V93, P15051 CAPLUS
- (18) Nielsen, L; Cancer Gene Ther 1997, V4, P129 CAPLUS
- (19) O'Connor, P; Cancer Res 1997, V57, P4285 CAPLUS
- (20) Pavletich, N; Genes Dev 1993, V7, P2556 CAPLUS
- (21) Prusiner, S; Science 1997, V278, P243
- (22) Rosenfeld, M; Neurology 1995, V45, P1533 CAPLUS
- (23) Sato, S; J Biol Chem 1996, V271, P635 CAPLUS
- (24) Selivanova, G; Nature Med 1997, V3, P632 CAPLUS
- (25) Stephen, C; J Mol Biol 1992, V225, P577 CAPLUS
- (26) Taubes, G; Science 1996, V271, P1493 CAPLUS
- (27) Wang, E; Cell 1989, V57, P379 CAPLUS

=> s 273921-61-2/rn

L5 1 273921-61-2/RN

=> d 15

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 273921-61-2 REGISTRY
CN 10H-Phenothiazine-10-propanamine, N-[1-(phenylmethyl)-4-piperidiny]-
(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H31 N3 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



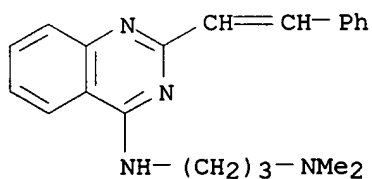
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s 273921-73-6/rn

L6 1 273921-73-6/RN

=> d 16

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 273921-73-6 REGISTRY
CN 1,3-Propanediamine, N,N-dimethyl-N'-[2-(2-phenylethenyl)-4-quinazolinyl]-
(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H24 N4
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



AN 95149780 EMBASE
 DN 1995149780
 TI Apoptosis and nuclear levels of p53 protein and proliferating cell nuclear antigen in human hepatoma cells cultured with tumor promoters.
 AU Kaneko Y.; Tsukamoto A.
 CS First Department of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan
 SO Cancer Letters, (1995) 91/1 (11-17).
 ISSN: 0304-3835 CODEN: CALEDQ
 CY Ireland
 DT Journal; Article
 FS 005 General Pathology and Pathological Anatomy
 016 Cancer
 021 Developmental Biology and Teratology
 030 Pharmacology
 037 Drug Literature Index
 LA English
 SL English
 AB **Anticancer drugs** etoposide and mitomycin C **increased** nuclear **p53** protein and decreased proliferating cell nuclear antigen (PCNA) of PLC/PRF/5 human hepatoma cells. These changes were followed by DNA fragmentation and apoptosis. Teleocidin antagonized both apoptosis and alterations of nuclear **p53** protein and PCNA induced by these anti-cancer **drugs**. In contrast, thapsigargin antagonized only **drug**-induced nuclear accumulation of **p53** protein. Therefore, the inhibition of apoptosis appears not to be the common mechanism of tumor promotion. Both tumor promoters suppressed the **increase** in nuclear **p53** protein, suggesting that an inadequate DNA repair due to the reduced nuclear accumulation of **p53** protein might be playing important role in enhancing carcinogenesis.
 CT Medical Descriptors:
 *apoptosis
 *hepatoma cell
 *tumor promotion: ET, etiology
 article
 cancer cell culture
 carcinogenesis: ET, etiology
 controlled study
 dna repair
 flow cytometry
 human
 human cell
 immunoblotting
 letter
 priority journal
 Drug Descriptors:
 *cycline: EC, endogenous compound
 *protein p53: EC, endogenous compound
 antineoplastic agent: PD, pharmacology
 cell protein: EC, endogenous compound
 dna fragment: EC, endogenous compound
 etoposide: PD, pharmacology
 mitomycin c: PD, pharmacology
 teleocidin
 thapsigargin
 tumor promoter
 RN (etoposide) 33419-42-0; (mitomycin c) 50-07-7, 74349-48-7; (teleocidin) 78474-55-2; (thapsigargin) 67526-95-8

=>

conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> s 58-40-2/rn

L1 1 58-40-2/RN

=> d 11

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 58-40-2 REGISTRY

CN 10H-Phenothiazine-10-propanamine, N,N-dimethyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phenothiazine, 10-[3-(dimethylamino)propyl]- (8CI)

OTHER NAMES:

CN 10-[3-(Dimethylamino)propyl]phenothiazine

CN 3276RP

CN A 145

CN Ampazine

CN Berophen

CN Esparin

CN Liranol

CN N-(3-Dimethylaminopropyl)phenothiazine

CN Neo-Hibernex

CN Prazin

CN Prazine

CN Promazine

CN Promwill

CN Protactyl

CN Romtiazin

CN RP 3276

CN Sinophenin

CN Tomil

CN Verophen

CN Wy 1094

FS 3D CONCORD

MF C17 H20 N2 S

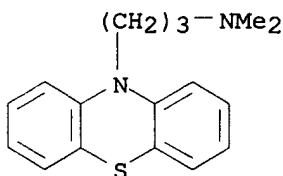
CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)



992 REFERENCES IN FILE CA (1967 TO DATE)

40 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

992 REFERENCES IN FILE CAPLUS (1967 TO DATE)

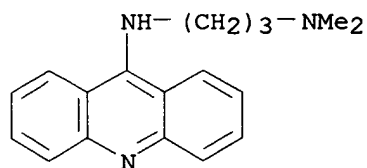
29 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s 13365-37-2/rn

L2 1 13365-37-2/RN

=> d 12

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 13365-37-2 REGISTRY
CN 1,3-Propanediamine, N'-9-acridinyl-N,N-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acridine, 9-[[3-(dimethylamino)propyl]amino]- (8CI)
OTHER NAMES:
CN 9-(3'-Dimethylaminopropylamino)acridine
CN 9-[[3-(Dimethylamino)propyl]amino]acridine
DR 23002-08-6
MF C18 H21 N3
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT,
MEDLINE,
RTECS*, TOXLINE, TOXLIT
(*File contains numerically searchable property data)



31 REFERENCES IN FILE CA (1967 TO DATE)
31 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d 25199-66-1/rn

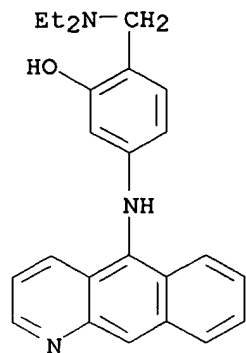
'25199-66-1' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'
The saved name for a query (or structure or screen set) must end with '/Q'. The saved name for an answer set must end with '/A'. The saved name for an L# list must end with '/L'. SDI request names must end with '/S'. To see a list of all saved query, answer set,, and L# list names for this loginid, enter "DISPLAY SAVED" at an arrow prompt (=>). Enter "DISPLAY SAVED/S" to see a list of SDI request names. Enter "DISPLAY SAVED/B" to see a list of BATCH search requests.

=> s 259199-66-1/rn

L3 1 259199-66-1/RN

=> d 13

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 259199-66-1 REGISTRY
CN Phenol, 5-(benzo[g]quinolin-5-ylamino)-2-[(diethylamino)methyl]- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN CP 257042
FS 3D CONCORD
MF C24 H25 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s127136-38-3

S127136-38-3 IS NOT A RECOGNIZED COMMAND

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"HELP COMMANDS" at an arrow prompt (=>).

=> s 127136-38-3/rn

L4 1 127136-38-3/RN

=> d 14

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 127136-38-3 REGISTRY

CN 1-Piperazineethanol, 4-[4-(benzo[g]quinolin-4-ylamino)phenyl]- (9CI) (CA
INDEX NAME)

OTHER CA INDEX NAMES:

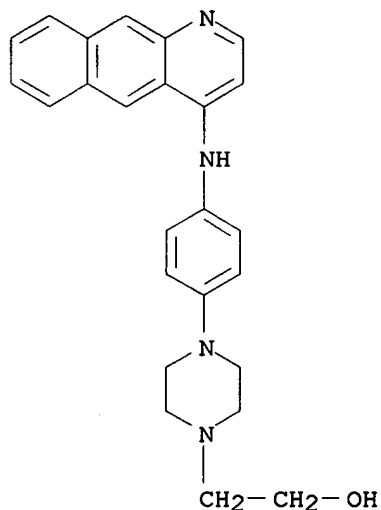
CN Benzo[g]quinoline, 1-piperazineethanol deriv.

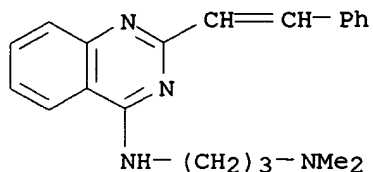
FS 3D CONCORD

MF C25 H26 N4 O

SR CA

LC STN Files: CA, CAPLUS, CHEMCATS, TOXLINE, TOXLIT





1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus

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	ENTRY	SESSION
FULL ESTIMATED COST	11.17	11.32

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FILE COVERS 1947 - 28 Jun 2001 VOL 135 ISS 1
FILE LAST UPDATED: 27 Jun 2001 (20010627/ED)

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The CA Lexicon is now available in the Controlled Term (/CT) field. Enter HELP LEXICON for full details.

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=> s 16

L7 1 L6

=> d 17 all

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
AN 2000:383903 CAPLUS
DN 133:26844
TI Methods and compositions using hydrophobic group- and cationic group-containing compounds for restoring conformational stability of a protein of the p53 family

IN Coffey, Heather Anne; Connell, Richard Damian; Foster, Barbara Ann;
 Rastinejad, Farzan
 PA Pfizer Products Inc., USA
 SO PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 1-6 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032175	A2	20000608	WO 1999-IB1916	19991201
	WO 2000032175	A3	20000803		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRAI US 1998-110542 P 19981202

OS MARPAT 133:26844

AB The invention provides pharmaceutical compds. capable of interacting with mutant and nonmutant forms of cancer-related regulatory proteins such that

the mutant protein regains the capacity to properly interact with other macromols., thereby restoring or stabilizing all or a portion of its wild type activity. Regulatory proteins include members of the p53 protein family, e.g. p53, p63 and p73. The compds. of the invention are useful for cancer treatment. Methods for screening for such pharmacol. compds. are also provided. Compds. of the invention contain a hydrophobic group (e.g. a planar polycyclic group) and a cationic group (preferably an amine) joined by a linker.

ST polycyclic amine compd p53 conformation stabilization; cancer treatment p53 conformation stabilizing compd; screening antitumor p53 conformation stabilizing compd

IT Protein motifs
 (DNA-binding domain; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT DNA
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (DNA-binding domain; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Animal cell line
 (H1299; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Animal cell line
 (SaOS-2; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Antitumor agents
 (carcinoma, DLD-1 cell; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT DNA
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (damage; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Temperature effects, biological
 (heat, p53 DNA-binding domain thermolability; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Alleles
 Antitumor agents
 Molecular association

Mutation
 Stabilizing agents
 Structure-activity relationship
 (hydrophobic group- and cationic group-contg. compds. for restoring
 p53-family protein conformational stability)
 IT p53 (protein)
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (hydrophobic group- and cationic group-contg. compds. for restoring
 p53-family protein conformational stability)
 IT Antitumor agents
 (melanoma, A375.S2 cell; hydrophobic group- and cationic group-contg.
 compds. for restoring p53-family protein conformational stability)
 IT Mutation
 (missense; hydrophobic group- and cationic group-contg. compds. for
 restoring p53-family protein conformational stability)
 IT Cyclin dependent kinase inhibitors
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (p21CIP1/WAF1; hydrophobic group- and cationic group-contg. compds.
 for
 restoring p53-family protein conformational stability)
 IT Proteins, specific or class
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (p63; hydrophobic group- and cationic group-contg. compds. for
 restoring p53-family protein conformational stability)
 IT Proteins, specific or class
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (p73; hydrophobic group- and cationic group-contg. compds. for
 restoring p53-family protein conformational stability)
 IT Conformation
 (protein; hydrophobic group- and cationic group-contg. compds. for
 restoring p53-family protein conformational stability)
 IT 58-40-2 84-96-8 13365-37-2 36945-50-3 74151-33-0 103395-43-3
 127136-38-3 259199-65-0 259199-66-1 273921-61-2 273921-62-3
 273921-63-4 273921-64-5 273921-65-6 273921-66-7 273921-67-8
 273921-68-9 273921-69-0 273921-70-3 273921-71-4 273921-72-5
273921-73-6
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hydrophobic group- and cationic group-contg. compds. for restoring
 p53-family protein conformational stability)

=>

---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	2.77	14.09
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.59	-0.59

STN INTERNATIONAL LOGOFF AT 10:20:52 ON 28 JUN 2001

AN 2000:383903 CAPLUS
 DN 133:26844
 TI Methods and compositions using hydrophobic group- and cationic
 group-containing compounds for restoring conformational stability of a
 protein of the p53 family
 IN Coffey, Heather Anne; Connell, Richard Damian; Foster, Barbara Ann;
 Rastinejad, Farzan
 PA Pfizer Products Inc., USA
 SO PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 1-6 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032175	A2	20000608	WO 1999-IB1916	19991201
	WO 2000032175	A3	20000803		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRAI	US 1998-110542	P	19981202		

OS MARPAT 133:26844
 AB The invention provides pharmaceutical compds. capable of interacting with
 mutant and nonmutant forms of cancer-related regulatory proteins such
 that the mutant protein regains the capacity to properly interact with other
 macromols., thereby restoring or stabilizing all or a portion of its wild
 type activity. Regulatory proteins include members of the p53 protein
 family, e.g. p53, p63 and p73. The compds. of the invention are useful
 for cancer treatment. Methods for screening for such pharmacol. compds.
 are also provided. Compds. of the invention contain a hydrophobic group
 (e.g. a planar polycyclic group) and a cationic group (preferably an
 amine) joined by a linker.
 ST polycyclic amine compd p53 conformation stabilization; cancer treatment
 p53 conformation stabilizing compd; screening antitumor p53 conformation
 stabilizing compd
 IT Protein motifs
 (DNA-binding domain; hydrophobic group- and cationic group-contg.
 compds. for restoring p53-family protein conformational stability)
 IT DNA
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (DNA-binding domain; hydrophobic group- and cationic group-contg.)

compds. for restoring p53-family protein conformational stability)

IT Animal cell line
(H1299; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Animal cell line
(SaOS-2; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Antitumor agents
(carcinoma, DLD-1 cell; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(damage; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Temperature effects, biological
(heat, p53 DNA-binding domain thermolability; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Alleles
Antitumor agents
Molecular association
Mutation
Stabilizing agents
Structure-activity relationship
(hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT p53 (protein)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Antitumor agents
(melanoma, A375.S2 cell; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Mutation
(missense; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Cyclin dependent kinase inhibitors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p21CIP1/WAF1; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p63; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p73; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT Conformation
(protein; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

IT 58-40-2 84-96-8 13365-37-2 36945-50-3 74151-33-0 103395-43-3
127136-38-3 259199-65-0 259199-66-1 273921-61-2
273921-62-3 273921-63-4 273921-64-5 273921-65-6 273921-66-7
273921-67-8 273921-68-9 273921-69-0 273921-70-3 273921-71-4
273921-72-5 273921-73-6
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)

AN 2000:6873 CAPLUS
 DN 132:175329
 TI Pharmacological rescue of mutant p53 conformation and function
 AU Foster, Barbara A.; Coffey, Heather A.; Morin, Michael J.; Rastinejad, Farzan
 CS Department of Genomics, Targets, and Cancer Research, Pfizer Central Research, Groton, CT, 06340, USA
 SO Science (Washington, D. C.) (1999), 286(5449), 2507-2510
 CODEN: SCIEAS; ISSN: 0036-8075
 PB American Association for the Advancement of Science
 DT Journal
 LA English
 CC 1-3 (Pharmacology)
 AB Compds. that stabilize the DNA binding domain of p53 in the active conformation were identified. These small synthetic mols. not only promoted the stability of wild-type p53 but also allowed mutant p53 to maintain an active conformation. A prototype compd. caused the accumulation of conformationally active p53 in cells with mutant p53, enabling it to activate transcription and to slow tumor growth in mice. With further work aimed at improving potency, this class of compds. may be developed into anticancer drugs of broad utility.
 ST CP31398 CP257042 p53 gene activation antitumor; conformation DNA binding domain p53 antitumor
 IT Conformation
 (DNA; pharmacol. rescue of mutant p53 conformation and function)
 IT Gene, animal
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (TP53; pharmacol. rescue of mutant p53 conformation and function)
 IT Structure-activity relationship
 (antitumor; pharmacol. rescue of mutant p53 conformation and function)
 IT Antitumor agents
 (pharmacol. rescue of mutant p53 conformation and function)
 IT 259199-65-0, CP 31398 259199-66-1, CP 257042
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (pharmacol. rescue of mutant p53 conformation and function)
 RE.CNT 27
 RE
 (1) Bartek, J; Oncogene 1990, V5, P893 CAPLUS
 (2) Bullock, N; Proc Natl Acad Sci USA 1997, V94, P14338
 (3) Chen, J; Oncogene 1993, V8, P2159 CAPLUS
 (4) Cho, Y; Science 1994, V265, P346 CAPLUS
 (5) Daniels, D; J Mol Biol 1994, V243, P639 CAPLUS
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 (9) Gamble, J; Virology 1988, V162, P452 CAPLUS
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 (12) Hollstein, M; Nucleic Acids Res 1994, V22, P3551 CAPLUS
 (13) Hupp, T; Cell 1995, V83, P237 CAPLUS
 (14) Kern, S; Science 1991, V252, P1708 CAPLUS
 (15) Legros, Y; Oncogene 1994, V9, P3689 CAPLUS
 (16) Milner, J; Oncogene 1990, V5, P1683 CAPLUS
 (17) Miroy, G; Proc Natl Acad Sci USA 1996, V93, P15051 CAPLUS
 (18) Nielsen, L; Cancer Gene Ther 1997, V4, P129 CAPLUS
 (19) O'Connor, P; Cancer Res 1997, V57, P4285 CAPLUS
 (20) Pavletich, N; Genes Dev 1993, V7, P2556 CAPLUS
 (21) Prusiner, S; Science 1997, V278, P243
 (22) Rosenfeld, M; Neurology 1995, V45, P1533 CAPLUS
 (23) Sato, S; J Biol Chem 1996, V271, P635 CAPLUS
 (24) Selivanova, G; Nature Med 1997, V3, P632 CAPLUS
 (25) Stephen, C; J Mol Biol 1992, V225, P577 CAPLUS
 (26) Taubes, G; Science 1996, V271, P1493 CAPLUS
 (27) Wang, E; Cell 1989, V57, P379 CAPLUS

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 PA Pfizer Products Inc., USA
 SO PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 1-6 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032175	A2	20000608	WO 1999-IB1916	19991201
	WO 2000032175	A3	20000803		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1998-110542	P	19981202		
OS	MARPAT 133:26844				
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IT	Protein motifs (DNA-binding domain; hydrophobic group- and cationic group-contg. compds. for restoring p53-family protein conformational stability)				
IT	DNA RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (DNA-binding domain; hydrophobic group- and cationic group-contg.)				

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(H1299; hydrophobic group- and cationic group-contg. comps. for restoring p53-family protein conformational stability)

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(heat, p53 DNA-binding domain thermolability; hydrophobic group- and cationic group-contg. comps. for restoring p53-family protein conformational stability)

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Antitumor agents
Molecular association
Mutation
Stabilizing agents
Structure-activity relationship
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RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
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for

IT Proteins, specific or class
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(p63; hydrophobic group- and cationic group-contg. comps. for restoring p53-family protein conformational stability)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
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AN 2000:6873 CAPLUS

DN 132:175329

TI Pharmacological rescue of mutant p53 conformation and function

AU Foster, Barbara A.; Coffey, Heather A.; Morin, Michael J.; Rastinejad, Farzan

CS Department of Genomics, Targets, and Cancer Research, Pfizer Central Research, Groton, CT, 06340, USA

SO Science (Washington, D. C.) (1999), 286(5449), 2507-2510
CODEN: SCIEAS; ISSN: 0036-8075

PB American Association for the Advancement of Science

DT Journal

LA English

CC 1-3 (Pharmacology)

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be developed into anticancer drugs of broad utility.

ST CP31398 CP257042 p53 gene activation antitumor; conformation DNA binding domain p53 antitumor

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(DNA; pharmacol. rescue of mutant p53 conformation and function)

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(TP53; pharmacol. rescue of mutant p53 conformation and function)

IT Structure-activity relationship

(antitumor; pharmacol. rescue of mutant p53 conformation and function)

IT Antitumor agents

(pharmacol. rescue of mutant p53 conformation and function)

IT 259199-65-0, CP 31398 259199-66-1, CP 257042

RL: BAC (Biological activity or effector, except adverse); BIOL

(Biological study)

(pharmacol. rescue of mutant p53 conformation and function)

RE.CNT 27

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- (1) Bartek, J; Oncogene 1990, V5, P893 CAPLUS
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